

Amendments to the Claims:

The following listing reflects amendments to the claims and replaces all prior versions and listings of claims in this application.

1. (Currently Amended) A ~~substantially~~ hydrophilic polymer-peptide conjugate comprising ~~an analgesic~~ a peptide that is either biphalin or [D-Pen², D-Pen⁵] enkephalin (DPDPE) covalently linked to a water-soluble, ~~nonpeptide~~ polymer selected from the group consisting of poly(ethylene glycol), copolymers of ethylene glycol and propylene glycol, poly(vinyl alcohol), poly(alkylene oxides), poly(oxyethylated polyols), poly(olefinic alcohols), poly(acryloyl morpholine), poly(vinylpyrrolidone), poly(oxazoline), dextran, and poly(hydroxyethyl methacrylate), ~~wherein said conjugate, when administered into the blood circulation of a mammal, can transport across the blood-brain barrier.~~

2. (Currently Amended) The conjugate of Claim 1, which, when administered ~~in~~ to the blood circulation of a mammal, has an extended duration of analgesic effect as- when compared to ~~the native peptide~~ the corresponding unconjugated peptide.

3. (Currently Amended) The conjugate of Claim 1, wherein said water-soluble, ~~nonpeptide~~ polymer is ~~further characterized by the absence of~~ absent one or more lipophilic moieties.

4. Canceled.

5. (Currently Amended) The conjugate of Claim 1, ~~further characterized by the absence of~~ absent noncovalent bonds.

6. (Original) The conjugate of Claim 1, wherein said peptide is covalently linked to at least one terminus of said polymer.

7. (Currently Amended) The conjugate of Claim 1, wherein said peptide is covalently linked at ~~one of its~~ an N-termini terminus to said polymer.

8. (Currently Amended) The conjugate of Claim 1, wherein said water-soluble, ~~nonpeptidic~~ polymer is polyethylene glycol or a copolymer of polyethylene glycol and polypropylene glycol.

9. (Currently Amended) The conjugate of Claim 1, wherein said water-soluble ~~nonpeptidic~~ polymer is polyethylene glycol.

10. (Original) The conjugate of Claim 9, wherein said polyethylene glycol is selected from the group consisting of monomethoxypolyethylene glycol, branched polyethylene glycol, polyethylene glycol with degradable linkages in the backbone, homobifunctional polyethylene glycol, heterobifunctional polyethylene glycol, multi-arm polyethylene glycol, pendant polyethylene glycol, and forked polyethylene glycol.

11. (Currently Amended) The conjugate of Claim 1, wherein said peptide is conjugated to a single at least one polyethylene glycol molecule.

12. (Currently Amended) The conjugate of Claim 1, ~~wherein said~~ comprising biphalin ~~has covalently attached to two polyethylene glycol moieties covalently attached.~~

13. (Currently Amended) The conjugate of Claim 1 wherein said ~~nonpeptidic~~ polymer is polyethylene glycol having a nominal average molecular weight of about 200 daltons to about ~~100,000~~ 40,000 daltons.

14. (Original) The conjugate of Claim 13 wherein said polyethylene glycol has a nominal average molecular weight of about 1,000 daltons to about 40,000 daltons.

15. (Original) The conjugate of Claim 13 wherein said polyethylene glycol has a nominal average molecular weight of 2,000 daltons.

16. (Original) A pharmaceutical composition comprising a conjugate according to Claim 1 and a pharmaceutically acceptable carrier.

17. (Currently Amended) The conjugate of Claim 1 further comprising a neuroactive agent, which may be the same or different from said peptide, conjugated to said ~~non-peptidic~~ polymer.

18. (Currently Amended) The conjugate of Claim 17 ~~4~~, wherein said polymer is a linear polymer having a first terminus covalently attached to said peptide and a second terminus covalently attached to said ~~further characterized by a dumbbell structure and further comprising a neuroactive agent, which may be the same or different from said peptide, conjugated to said nonpeptidic polymer.~~

19. (Currently Amended) The conjugate of Claim 1, further comprising doxorubicin or an imaging or diagnostic agent conjugated to said ~~nonpeptidic~~ polymer.

20. (Canceled).

21. (Currently Amended) The conjugate of Claim 1, A substantially hydrophilic conjugate comprising an analgesic peptide that is either biphalin [D-Pen², D-Pen⁵] or enkephalin (DPDPE) covalently linked to a water soluble, nonpeptidic polymer in a reaction mixture in which said peptide and nonpeptidic polymer are present as reagents, and wherein said polymer is selected from the group consisting of poly(ethylene glycol), copolymers of ethylene glycol and propylene glycol, poly(vinyl alcohol), poly(alkylene oxides), poly(oxyethylated polyols), poly(olefinic alcohols), poly(acryloyl morpholine), poly(vinylpyrrolidone), poly(oxazoline), dextran, poly(hydroxyethyl methacrylate), ~~said conjugate is characterized by the absence of noneovent bonds and , which, when administered into the blood circulation of a mammal, is transported ean transport~~ across the blood-brain barrier thereof of a mammal, wherein said nonpeptidic polymer is absent lipophilic moieties.

22. (Canceled)

23. (Currently Amended) The conjugate of Claim 22 1 wherein said peptide is biphalin.

24. (Currently Amended) The conjugate of Claim 23 1 wherein said peptide is DPDPE.

25. (Canceled)

26. (Currently Amended) A hydrophilic The conjugate of claim 1, comprising an analgesic peptide that is either biphalin [D-Pen², D-Pen⁵] or enkephalin (DPDPE) covalently linked to a water soluble, nonpeptidic polymer in a reaction mixture in which said peptide and said nonpeptidic polymer are present as reagents, and wherein said polymer is selected from the

~~group consisting of poly(ethylene glycol), copolymers of ethylene glycol and propylene glycol, poly(vinyl alcohol), poly(alkylene oxides), poly(oxyethylated polyols), poly(olefinic alcohols, poly(acryloyl morpholine), poly(vinylpyrrolidone), poly(oxazoline), dextran, poly(hydroxyethyl methacrylate); said conjugate is characterized by the absence of noncovalent bonds and, when administered into the blood circulation of a mammal, can transport across the blood-brain barrier of a mammal, wherein said nonpeptide polymer is absent fatty acids and glycolipids.~~

27. (Currently Amended) The conjugate of Claim 1, wherein said ~~non-peptide~~ polymer is poly(ethylene glycol) having the ~~general~~ formula $-\text{CH}_2\text{CH}_2\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2-$, wherein n ranges from about 10 to 2000.

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